Remarks

Claims 15, 17-20, 22, 24-27, 29, 31-34, 36, 38-41, and 43 are pending in the application.

Claims 1-14 and 44-54 have been canceled without prejudice as drawn to a non-elected invention. The Applicant expressly reserves the right to prosecute the canceled claims in a divisional application claiming the benefit of priority to the instant application and its predecessor(s). 35 USC § 121.

Claims 16, 21, 23, 28, 30, 35, 37, and 42 have been canceled without prejudice. The Applicant expressly reserves the right to prosecute the canceled claims in a continuing application claiming the benefit of priority to the instant application and its predecessor(s). 35 USC § 120. Further, the cancellation of claims should not be construed to be an acquiescence to any of the rejections. Rather, except where another rationale is explicitly provided, the claims are being canceled solely to expedite the prosecution of the above-identified application.

Claims 15, 22, 29, 36, and 43 have been amended. Support for the claim amendments can be found throughout the application, including the claims as originally filed. Importantly, no new matter has been added to the claims. Further, the amendments to the claims should not be construed to be an acquiescence to any of the rejections. Rather, except where another rationale is explicitly provided, the amendments to the claims are being made solely to expedite the prosecution of the above-identified application. Moreover, the Applicant reserves the right to further prosecute the same or similar claims in subsequent patent applications claiming the benefit of priority to the instant application. 35 USC § 120.

Objections to the Specification

The Examiner objected to the Specification, page 28, first paragraph, because it contains an embedded hyperlink. Therefore, the Applicants have amended this paragraph to remove the embedded hyperlink. Accordingly, the Applicants respectfully contends that Specification conforms with all relevant statutes, regulations, and procedures.

Claim Objections

The Examiner objected to claim 43 because it depends on non-elected claims 1 and 8. Accordingly, the Applicants have amended claim 43, removing the dependency to which the Examiner objected.

The Examiner also objected to claim 43 under 37 CFR § 1.75(c), based on the presence of the word "and" in the preamble of the multiply dependent claim. Accordingly, the Applicants have amended the preamble of claim 43, replacing "and" with "or" and making grammatical changes necessitated by the amendment.

Claim Rejections Based on 35 USC § 112¶1

Claims 15-20, 22-27, and 43 stand rejected under 35 U.S.C. § 112¶1 based on the Examiner's contention that they contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The Applicants respectfully traverse this rejection.

Independent claims 15 and 22 have been amended to define the "scaffold" as a pyrazine moiety. Further, the "pharmacophore units" and "modifiers" have been defined using art-recognized chemical groups and biological terms, respectively. Representative examples exist throughout the Exemplification section of the specification. *See* pages 39-44 and Figures 4-12. Consequently, the Applicants respectfully submit that pending claims 15, 17-20, 22, 24-27, 29, 31-34, 36, 38-41, and 43 satisfy both the written description and enablement requirements of 35 U.S.C. § 112¶1.

Accordingly, the Applicants respectfully request the withdrawal of the claim rejections based on 35 U.S.C. § 112¶1.

Claim Rejections Based on 35 USC § 112¶2

Claims 20 and 27 stand rejected under 35 U.S.C. § 112¶2 based on the Examiner's contention that they are indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Applicants respectfully traverse this rejection.

Claims 15 and 22, from which claims 20 and 27 depend, have been amended to label the biologically active groups as pharmacophoric units defined in terms of R_1, R_2, and R_3. Support for these amendments can be found on page 18 of the specification. Consequently, the Applicants respectfully submit that amended claims 20 and 27 are definite.

Accordingly, the Applicants respectfully request the withdrawal of the claim rejections based on 35 U.S.C. § 112¶2.

Claim Rejections Based on 35 USC § 102(b)

Gootjes and Gootjes

Claims 15-20, 22-27 and 43 stand rejected under 35 U.S.C. 102(b) as being anticipated by either Gootjes (U.S. Patent No. 4,202,896; "Gootjes 1") or Gootjes (U.S. Patent No. 4,265,894; "Gootjes 2"). The Applicants respectfully traverse this rejection.

The present invention relates to a polypharmacophore comprising three units bound together through a central scaffold moiety. This joining of the three units represents a departure from the prior art where three individual biologically active agents are administered as a mixture. Gootjes 1 and Gootjes 2 both fail to disclose compounds where three pharmacophoric units are covalently bound together through a scaffold moiety.

In fact, Gootjes 1 and Gootjes 2 both define "X" as a series of methylene groups or a vinyl methylene groups. Both definitions would require R_1 in the present invention to be H in order for either Gootjes 1 or Gootjes 2 to anticipate the present claims. Independent claims 15 and 22 have been amended to define R_1 as aryl, aralkyl, aralkenyl, $-CO_2H$, amido, and ester; pertinently, this group does not include H. Because R_1 can not be H, Gootjes 1 or Gootjes 2 do not anticipate the pending claims.

Moldt et al.

Claims 15-20, 22-27 and 43 stand rejected under 35 U.S.C. § 102(b) based on the Examiner's contention that they are anticipated by Moldt et al. (U.S. Patent No. 5,369,113). The Applicants respectfully traverse this rejection.

Moldt et al. discloses a number of tropane derivatives as dopamine reuptake inhibitors. Independent claims 15 and 22 have been amended to define the polypharmacophores as comprising a pyrazine ring. Because the polypharmacophores of the present invention are not tropane derivatives, the Applicants respectfully submit that Moldt et al. does not anticipate any of the pending claims.

Cordi et al.

Claims 15-20, 22-27 and 43 stand rejected under 35 U.S.C. § 102(b) based on the Examiner's contention that they are anticipated by Cordi et al. (U.S. Patent No. 5,208,260). The Applicants respectfully traverse this rejection.

Cordi et al. discloses a number of vinyl glycine derivatives for use in memory and learning enhancement or for treatment of a cognitive disorder. In Cordi et al., R^1 and R^2 are substituents bound to nitrogen. The definitions of R^1 and R^2 do not allow for a ring containing a second nitrogen atom. Therefore, the compounds in Cordi et al. do not comprise a pyrazine ring. Independent claims 15 and 22 have been amended such that the polypharmacophores comprise a pyrazine ring. Because the vinyl glycine derivatives of Cordi et al. do not comprise a pyrazine ring, the Applicants respectfully submit that Cordi et al. does not anticipate any of the claims.

Zeitlin et al.

Claims 15-20, 22-27 and 43 stand rejected under 35 U.S.C. § 102(b) based on the Examiner's contention that they are anticipated by Zeitlin et al. (U.S. Patent No. 5,733,756). The Applicants respectfully traverse this rejection.

Zeitlin et al. discloses a number of substituted piperidine compounds for use as intermediates in the synthesis of central nervous system stimulants. Independent claims 15 and 22 have been amended such that the polypharmacophores comprise a pyrazine ring. Because the intermediates disclosed in Zeitlin et al. do not comprise a pyrazine ring, the Applicants respectfully submit that Zeitlin et al. does not anticipate any of the pending claims.

Accordingly, the Applicants respectfully request the withdrawal of the claim rejections based on 35 U.S.C. § 102(b).

Claim Rejections Based on 35 USC § 103(a)

Claims 16 and 23 stand rejected under 35 U.S.C. § 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over any of Gootjes (U.S. Patent No. 4,202,896) or Gootjes (U.S. Patent No. 4,265,894) or Moldt et al. (U.S. Patent No. 5,369,113) or Cordi et al. (U.S. Patent No. 5,208,260) or Zeitlin et al. (U.S. Patent No. 5,733,756).

The Applicants respectfully submit that the cancellation of claims 16 and 23 has rendered this rejection moot.

Accordingly, the Applicants respectfully request the withdrawal of the claim rejections based on 35 U.S.C. § 103(a).

Conclusion

In view of the above amendments and remarks, the Applicants believe that the pending claims are in condition for allowance. If a telephone conversation with Applicant's Attorney would expedite prosecution of the application, the Examiner is urged to contact the undersigned. Marked-up versions of the amended paragraph of the Specification and the amended claims follow.

Respectfully submitted,
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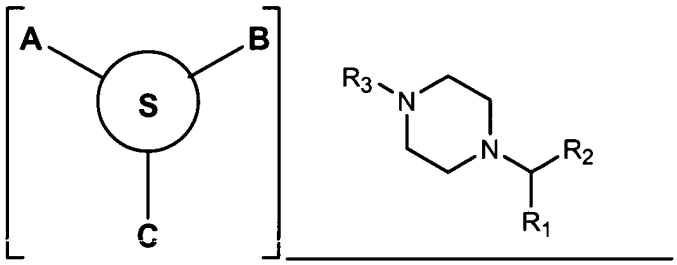
Marked-Up Version of Amended Paragraph of Specification Showing Changes Made

On page 28, the first full paragraph was amended as follows:

Furthermore, the methods of combinatorial chemistry are being brought to bear, e.g., [e,g,,] by G.L. Verdine at Harvard University, on the development of new peptidomimetics [(see, http://glviris.harvard.edu/frame_research.htm)]. For example, one embodiment of a so-called "peptide morphing" strategy focuses on the random generation of a library of peptide analogs that comprise a wide range of peptide bond substitutes.

Marked-Up Version of Amended Claims Showing Changes Made

15. **(amended)** A polypharmacophore [comprising the general] represented by formula **(II):**



(II)

wherein: [S comprises a scaffold unit; at least two of A, B, or C comprise a pharmacophore;]

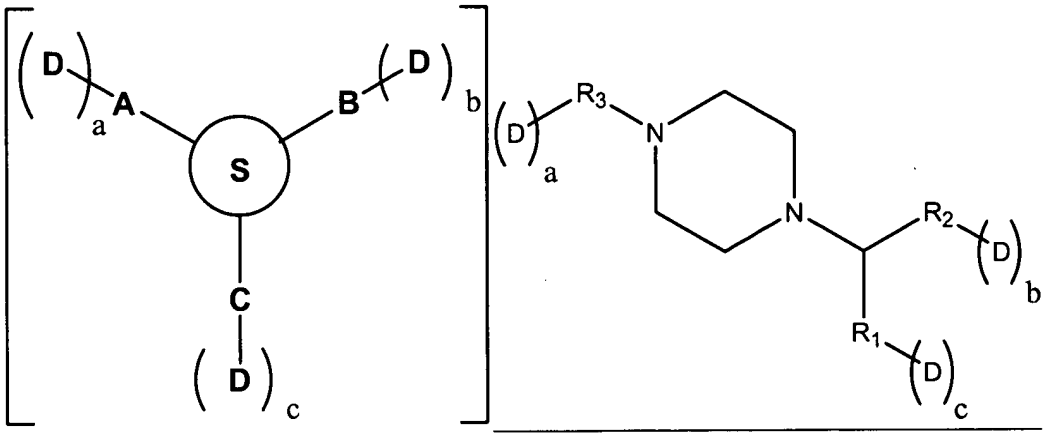
R_1 is selected from the group consisting of aryl, aralkyl, aralkenyl, $-CO_2H$, amido, and ester;

R_2 is selected from the group consisting of aralkyl and aralkenyl; and

R_3 is selected from the group consisting of aryl, amine, and ether; [and]

wherein one or none of [A, B, or C] R_1, R_2, or R_3 comprises a modifier unit selected from the group consisting of lipids, antibodies, lectins, sugars, steroids, hormones, proteins, biotin, folate, riboflavincarnitne, inositol, lipoic acid, niacin, pantothenic acid, thiamin, pyridoxal, ascorbic acid, heptens, epitopes, dsDNA fragments, and vitamins A, D, E, and K, whereby the polypharmacophore interacts with at least two biological targets.

22. **(amended)** A polypharmacophore [comprising the general] represented by formula **(IIA):**



(IIA)

wherein: [S comprises a scaffold unit; at least two of A, B, or C comprise a pharmacophore;]

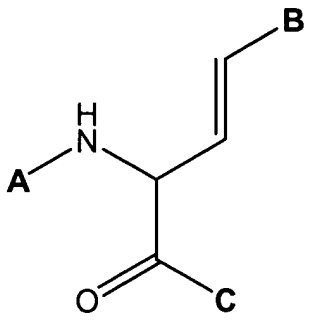
R_1 is selected from the group consisting of aryl, aralkyl, aralkenyl, CO_2H, amido, and ester;

R_2 is selected from the group consisting of aralkyl and aralkenyl; and

R_3 is selected from the group consisting of aryl, amine, and ether;

one or none of [A, B, or C] R_1, R_2, or R_3 comprises a modifier unit; and D comprises an additional modifier unit wherein the modifier units are selected from the group consisting of lipids, antibodies, lectins, sugars, steroids, hormones, proteins, biotin, folate, riboflavincarnitne, inositol, lipoic acid, niacin, pantothenic acid, thiamin, pyridoxal, ascorbic acid, heptens, epitopes, dsDNA fragments, and vitamins A, D, E, and K; and, wherein a, b, and c are each independently greater than or equal to zero, whereby the polypharmacophore interacts with at least two biological targets.

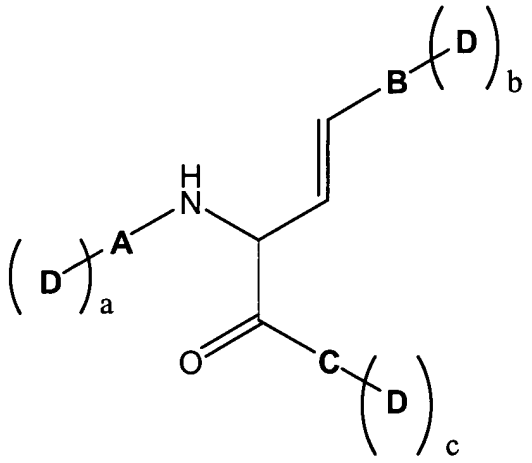
29. (**amended**) A polypharmacophore [comprising the] represented by formula **(III):**



(III)

wherein at least two of A, B, or C comprise a pharmacophore; and wherein one or none of A, B, or C comprise a modifier unit, whereby the polypharmacophore interacts with at least two biological targets.

36. **(amended)** A polypharmacophore [comprising the] represented by formula **(IIIA):**



(IIIA)

wherein at least two of A, B, or C comprise a pharmacophore; one or none of A, B, or C comprise a modifier unit; and D comprises an additional modifier unit, wherein a, b, and c are each independently greater than or equal to zero, whereby the polypharmacophore interacts with at least two biological targets.

43. **(amended)** A pharmaceutical composition, comprising:

a polypharmacophore of [any one of claims 1, 8,] claim 15, 22, 29, [and] or 36, or a pharmaceutically acceptable salt thereof; and

a pharmaceutically acceptable diluent or carrier.